

DNA fragments, wherein the cDNA or genomic DNA fragments in the pool of expression constructs are derived from an environmental sample comprising a plurality of species of donor organisms, and wherein the cDNA or genomic DNA fragments in each expression construct are operably-associated each with one or more regulatory regions that drives expression of genes encoded by the cDNA or genomic DNA fragments in an appropriate host organism.

28 (new). A combinatorial chimeric pathway gene expression library, comprising a pool of expression constructs, each expression construct containing randomly concatenated cDNA or genomic DNA fragments derived from an environmental sample comprising one or more species of donor organisms, in which the concatenated cDNA or genomic DNA fragments are operably-associated with one or more regulatory regions that drive expression of genes encoded by the concatenated cDNA or genomic DNA fragments in an appropriate host organism.

29 (new). A biased combinatorial gene expression library, comprising a pool of expression constructs, each expression construct containing cDNA or genomic DNA fragments preselected from a plurality of species of donor organisms derived from an environmental sample for a specific property, in which the cDNA or genomic DNA fragments are operably-associated with one or more regulatory regions that drive expression of genes encoded by the cDNA or genomic DNA fragments in an appropriate host organism.

30 (new). The gene expression library of claim 27, 28, or 29 wherein the environmental sample is a soil sample.

31 (new). The gene expression library of claim 27, 28, or 29 wherein the environmental sample is selected from the group consisting of deposits near hot springs, deposits near thermal vents, freshwater filtrates, marine sediments, estuarine sediments, or seawater filtrates.

32 (new). The gene expression library of claim 27, 28, or 29 wherein at least one of the cDNA or genomic DNA fragments comprises nucleotide sequences that encode for proteins or fragments thereof that are involved in secondary metabolism.

33 (new). The gene expression library of claim 27, 28, or 29 wherein at least one of the cDNA or genomic DNA fragments comprises nucleotide sequences that encode for proteins or fragments thereof that are involved in antibiotic biosynthesis.

Sub S 34 (new). The gene expression library of claim 27, 28, or 29 wherein at least one of the cDNA or genomic DNA fragments comprises nucleotide sequences that encode for proteins or fragments thereof that are involved in polyketide biosynthesis, peptide biosynthesis, glycoside biosynthesis, aminoglycoside biosynthesis, mevalonic acid biosynthesis, or glucose transfer systems.

35 (new). The gene expression library of claim 27, 28, or 29 wherein at least one of the cDNA or genomic DNA fragments comprises nucleotide sequences that encode for proteins or fragments thereof that are involved in the biosynthesis of beta-lactams, macrolides, alkaloids, bryostatins, carotenoids, steroids, or retinoids.

D 36 (new). The gene expression library of claim 27, 28, or 29 wherein the expression constructs are contained in host cells.

37 (new). The gene expression library of claim 30 wherein the expression constructs are contained in host cells.

38 (new). The gene expression library of claim 31 wherein the expression constructs are contained in host cells.

39 (new). The gene expression library of claim 32 wherein the expression constructs are contained in host cells.

40 (new). The gene expression library of claim 33 wherein the expression constructs are contained in host cells.

41 (new). The gene expression library of claim 34 wherein the expression constructs are contained in host cells.

42 (new). The gene expression library of claim 35 wherein the expression constructs are contained in host cells.

43 (new). The gene expression library of claim 27, 28, or 29 wherein the expression constructs comprises a plasmid vector, a phage vector, a viral vector, a cosmid vector, or an artificial chromosome.

44 (new). A biased combinatorial gene expression library, comprising a pool of expression constructs, each expression construct containing cDNA or genomic DNA fragments some of which are preselected from a plurality of species of donor organisms by hybridization of the cDNA or genomic DNA fragments to nucleic acid probes comprising nucleotide sequences that encode for proteins or fragments thereof that are involved in secondary metabolism, in which the cDNA or genomic DNA fragments are operably associated with one or more regulatory regions that drive expression of genes encoded by the cDNA or genomic DNA fragments in an appropriate host organism.

45 (new). The biased combinatorial gene expression library of claim 44 wherein some of the cDNA or genomic DNA fragments are preselected by hybridization of the cDNA or genomic fragments to nucleic acid probes comprising nucleotide sequences that encode for proteins or fragments thereof that are involved in polyketide biosynthesis, peptide biosynthesis, glycoside biosynthesis, aminoglycoside biosynthesis, mevalonic acid biosynthesis, or glucose transfer systems.

46 (new). The biased combinatorial gene expression library of claim 44 wherein some of the cDNA or genomic DNA fragments are preselected by hybridization of the cDNA or genomic DNA fragments to nucleic acid probes comprising nucleotide sequences that encode for proteins or fragments thereof that are involved in antibiotic biosynthesis.

47 (new). The biased combinatorial gene expression library of claim 44 wherein some of the cDNA or genomic DNA fragments are preselected by hybridization of the cDNA or genomic DNA fragments to nucleic acid probes comprising nucleotide

sequences that encode for proteins or fragments thereof that are involved in the biosynthesis of beta-lactams, macrolides, alkaloids, bryostatins, carotenoids, steroids, or retinoids.

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48 (new). The biased combinatorial gene expression library of claim 44 wherein some of the cDNA or genomic DNA fragments are preselected by hybridization of the cDNA or genomic DNA fragments to nucleic acid probes comprising nucleotide sequences that encode for proteins or fragments thereof that are involved in the biosynthesis of erythromycin, actinorhodin, thiostrepton, virginiamycin, valinomycin, actinomycin, tetracycline, oxytetracycline, puromycin, doxorubicin, taxol, chloramphenicol, nalidixic acid, mithramycin, novobiocin, vulpinic acid, usnic acid, kainic acid, podophyllotoxin, brevitoxin, camptothecin, or artemisinin.

49 (new). The biased combinatorial gene expression library of claim 44, 45, 46, 47, or 48 wherein the expression constructs are contained in host cells.

50 (new). The biased combinatorial gene expression library of claim 44, 45, 46, 47, or 48 wherein the expression constructs comprise a plasmid vector, a phage vector, a viral vector, a cosmid vector, or an artificial chromosome.

REMARKS

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The specification has been amended to include the accession number for the cosmid vector pPCos+ura.

Claims 22-24 have been canceled without prejudice. New claims 27-50 have been added to more particularly point out and distinctly claim that which Applicants regard as the invention. Applicants respectfully request the examination of the new claims which are directed to subject matter related to claims allowed and issued in the parent applications of the present application. The subject matter of the new claims is fully supported in the specification. In particular, support for new claims 27-32 and 44 is found in page 10, line 20 to page 11, line 8, page 25, line 33 to page 26, line 9, and page 62, lines 19-32. New claims 34 and 45 are supported in the specification at page 6, lines 28-34; page 25, line 23; page 53, line 18; page 63, lines 35-36; and page 64, lines 5-6. New claims 33, 35, 46 and 47 are supported at page 30, lines 5-9; page 29, line 12; page 29, line 21; page 49, line 14; and page 64, lines 5-6. New claim 48 are supported at page 29, lines 7-20; page 24, line 15; page 49,